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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,442	05/19/2005	Stina Roth	014975-119	8832

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EXAMINER	
POHNERT, STEVEN C	
ART UNIT	PAPER NUMBER
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/535,442	ROTH ET AL.	
	Examiner	Art Unit	
	Steven C. Pohnert	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 19-22* is/are pending in the application.

4a) Of the above claim(s) *6, 11,-15, 19-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-10 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 May 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/19/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Sequence Compliance

1. The application fails to comply with CFR 1.821(d), which states:

> (d)Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

For example, page 20 line 30 and Figure 1, contain a nucleic acid sequence. Applicant is required to check the rest of the disclosure for any other nucleic acid or protein sequences and list them in a sequence listing and identify them with a proper SEQ ID NO.

The specification must be amended to bring it into sequence compliance. **A response to this office action will be held non-compliant if the specification has not been amended to make it sequence compliant.**

Election/Restrictions

2. Applicant's election with traverse of group I, claims 1-13, the bacterial species Staphylococcus Aureus and SEQ ID NO 24 in the reply filed on 11/17/2006 is acknowledged. The traversal is on the ground(s) that the office has not fully apprehended the special technical feature represented by primers associated with SEQ ID NO: 76 and 77. This is not found persuasive because although Warren does not teach SEQ ID NO 76 and 77, he does teach SEQ ID NO 3 and 4. Which comprise functional fragments of SEQ ID NO 76 and 77. Specifically SEQ ID NO 3 of Warren

teaches ATA, which are 3 of the last 4 nucleotides of SEQ ID NO 76 and SEQ ID NO 4 of Warren CCGC, which are 4 of the last 7 nucleotides of SEQ ID NO 77. The 3' end is the functional end of a primer. As Warren teaches functional fragments of SEQ ID No 76 and 77, the claimed inventions lack a special technical feature over the prior art and thus lack unity.

3. Claims 6, 11-15, 19-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11/17/2006.

Claims 6, 11, and 12 are withdrawn as applicant elected SEQ ID NO 24 in claim 5, not the whole combination. Claims 6, 11, and 12 thus are beyond the scope of the elected invention.

4. The requirement is still deemed proper and is therefore made FINAL.

Drawings

5. The drawings are objected to because they contain nucleic acid sequences that are not identified by SEQ ID NOs. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as

"amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance. Alternatively, the description of the drawings can be modified to identify the sequences by SEQ ID NO.

Specification

6. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Page 17, lines 8-9 contain a hyperlink. The applicant must check the rest of the specification for other hyperlinks.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-5, 7-10, and 13 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5, 7-10, and 13 are indefinite because it lacks a positive active step relating back to the preamble. The preamble recites a method of detecting and identifying bacterial species, however the last positive active step is drawn to detecting the formation of possible hybridization complex. Therefore it is unclear as to whether the method is drawn to of detecting and identifying bacterial species or to detecting the formation of possible hybridization complex.

Claims 1-5, 7-10, and 13 are indefinite in that they recite "desired combination of oligonucleotide probe sequences". It is unclear what a desired combination is.

Claims 1-5, 7-10, and 13 are indefinite in that they recite "said sequences". It is unclear if the desired sequence is the primer sequence or the conserved regions.

Claims 1-5, 7-10, and 13 are indefinite in that they recite "possible hybridization complexes". It is unclear if the hybridization complex is the hypervariable region with the primers or the hypervariable region with the probes.

Claim 4 is indefinite in that it recites a numerical range that falls within a broader range. See MPEP 2173.05(c) I.

> Use of a narrow numerical range that falls within a broader range in the same claim may render the claim indefinite when the boundaries of the claim are not discernible. Description of examples and preferences is properly set forth in the specification rather than in a single claim. A narrower range or preferred

embodiment may also be set forth in another independent claim or in a dependent claim. If stated in a single claim, examples and preferences lead to confusion over the intended scope of the claim. In those instances where it is not clear whether the claimed narrower range is a limitation, a rejection under 35 U.S.C. 112, second paragraph should be made.

9. Claim 8 recites the limitation "the DNA isolated" in lines 1 and 2. There is insufficient antecedent basis for this limitation in the claim. Claim 1 teaches amplification of isolated DNA.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-2, and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Haung (US Patent 5,645,994, Issued 1997).

Claim 1 recites, "a functional fragments" in reference to SEQ ID NOs 76 and 77. The specification does not specifically define a functional fragment, thus a functional fragment is broadly interpreted to be at least a single nucleotide.

With regards to claim 1, Huang teaches a method of identifying species of bacteria in a sample by amplification with universal primers based on consensus amino acid sequences which flank variable amino acid sequences (see abstract). Haung further teaches a method of designing universal primer that amplify parE and gyrB (see column 6 lines 28-65), these universal primers would identify the sequences that SEQ ID NO 76 and 77 would identify and comprise functional fragments of SEQ ID NO 76

and 77. Haung further teaches the use of universal primer compositions to amplify gyrB and parE sequences (see column 14, lines 16-19). Haung further teaches the use of nested primers to specifically distinguish between closely related species (see column 15 lines 27-35). The nested probes are thus the equivalents of the probes claimed.

Haung thus teaches a method of amplification and identification of bacterial species by hybridizing of nested primers with amplification products from universal primers. The nested primers of Haung are used to identify specific species of bacteria, and are thus equivalent to the probes of the claim. Haung's method of nested PCR is contacting amplification products with a desired number of oligonucleotide probes, and detection of hybridization complexes would be the presence of extension products.

With regards to claim 2, Haung further teaches the use of universal primer compositions to amplify gyrB and parE sequences due to their sequence similarities (see column 14, lines 16-19). Haung further teaches identification of legionella pneumophila (SEQ ID NO 70), which is a bacteria that infects the respiratory tract.

With regards to claim 4, Haung et al teaches the use of primers of 15 to 36 nucleotides in length (see column 7, lines 22-25).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claim 3, 7, 8, 10, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haung (US Patent 5645994, Issued 1997) in view of Voelker (US patent publication 2004/0048281, filed March 23, 2001).

Huang teaches a method of identifying species in a sample by amplification with universal primers based on consensus amino acid sequences which flank variable amino acid sequences (see abstract). Haung further teaches a method of designing universal primer (see column 6 lines 28-65); these universal primers are minimally, functional fragments that identify the sequence that SEQ ID NO 76 and 77 detect. Haung further teaches the use of universal primer compositions to amplify gyrB and parE sequences (see column 14, lines 16-19). Haung further teaches the use of nested primers to specifically distinguish between closely related species (see column 15 lines 27-35).

Haung does not teach the amplification of the hypervariable region of gyrB or parE in Staphylococcus aureus. Haung does not teach the use of a solid support.

However, Voelker et al teaches amplification of gram-positive bacteria, Staphylococcus aureus gyrB (see figure 1B, lane 3, and paragraph 0025) and parE (see figure 2B, lane 3, and paragraph 0026). Voelker teaches that most clinical samples are from gram-positive bacteria (see paragraph 0004). Voelker teaches the use of degenerate primers for the identification of quinolone resistance determining regions across phylogenetic ranges of prokaryotes (see paragraph 0001, last sentence) for diagnosis, prognosis, therapy and drug discovery (see paragraph 0024).

Further, Voelker et al teaches, "a solid surface on which is immobilized at pre-defined regions thereon a plurality of defined oligonucleotide/polynucleotide sequences for hybridization and identification." The solid surface with immobilized probes is a microarray (see paragraph 0024).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the Haung method of detecting bacterial species to amplify gyrB and parE to identify Staphylococcus aureus and use a solid support as taught by Voelker. The ordinary artisan would be motivated improve Haung's method of bacterial detection to identify Staphylococcus aureus and use solid supports as taught Voelker because Voelker teaches gram positive bacteria are the most clinically relevant. This would allow proper diagnosis and treatment of these gram-positive bacteria. Further the use of the probes on solid supports as Voelker teaches would decrease the use of reagents and increase the speed of detection.

13. Claims 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Haung (US Patent 5645994, Issued 1997) in view of Hogan et al (US Patent 5541308) and Hopewell et al (Journal of Bacteriology (1990), volume 172, pages 3481-3484)

Huang teaches a method of identifying species in a sample by amplification with universal primers based on consensus amino acid sequences, which flank variable amino acid sequences (see abstract). Haung further teaches a method of designing universal primer (see column 6 lines 28-65), these universal primers are minimally, functional fragments of SEQ ID NO 76 and 77. Haung further teaches the use of

universal primer compositions to amplify gyrB and parE sequences (see column 14, lines 16-19

Haung does not teach the probe of the comprising all or a portion of SEQ ID NO 24.

However, Hogan et al teaches probe design for detection of specific sequences (see abstract). Hogan teaches identification of variable regions (see column 6, lines 3-55). Hogan teaches alignment of these variable regions (see column 6 line 67—column 7, line 8). Hogan further teaches probes should be positioned to minimize stability of probe:nontarget hybrids, by avoiding GC rich regions and areas of frequent mutation (see column 7 lines 10-15). Hogan further teaches maximizing stability of probe target hybrid, by avoiding long AT sequences and terminating hybrids with G:C base pairing and the appropriate T_m(see column 7 lines 16-19). Hogan further teaches targeting sequences known to have secondary structure issues and probes that are self-complementary should be avoided (see column 7, lines 20-29).

Hopewell teaches sequence of Staphylococcus aureus gyrB, which comprises SEQ ID NO 24, (see figure 3B). Hopewell teaches that methicillin resistant Staphylococcus aureus are a major medical problem and this resistance is due to mutations in the DNA gyrase enzyme (see page 3481, 1st column, 1st paragraph).

Designing probes, which are equivalents to those taught in the art is routine experimentation. The prior art teaches the parameters and objectives involved in the selection of oligonucleotides that function as probes, see Hogan. Moreover there are many internet web sites that provide free downloadable software to aid in the selection

of probes drawn from genetic data recorded in a spreadsheet. The prior art is replete with guidance and information necessary to permit the ordinary artisan in the field of nucleic acid detection to design probes As discussed above, the ordinary artisan would be motivated to have designed and tested new probes to obtain additional oligonucleotides that function to detect specific hypervariable regions of bacteria and identify oligonucleotides with improved properties. The ordinary artisan would have a reasonable expectation of success of obtaining additional probes from within the sequences provided by Haung. Thus, for the reasons provided above, the ordinary artisan would have designed additional probes using the teachings in the art at the time the invention was made. The claimed SEQ ID NOs are obvious over the cited prior art, absent secondary considerations.

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the sequences taught by Hopewell and the probe design method of Hogan to make probes to detect bacterial species based on the gyrB. The ordinary artisan would thus design a probe comprising SEQ ID NO 24 or a functional fragment of SEQ ID NO 24. The ordinary artisan would be motivated to use the sequence taught by Hopewell to design probes by Hogan's method of probe design to identify mutations that result in methillicin resistance because Hopewell teaches this is a serious medical problem and proper identification would allow efficient treatment.

14. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Haung (US Patent 5645994, Issued 1997) and Voelker (US patent publication 2004/0048281,

filed March 23, 2001) as applied to claim7 above, and further in view of Southern et al (Nature Genetics supplement (1999), volume 21 pages 5-9).

The teachings of Haung in view of Voelker are set forth above.

Haung and Voelker teach the use of a solid support, however they do not teach the use of treated glass as a solid substrate.

Southern et al teach that treated glass is a preferred solid support as it allows the synthesis of oligonucleotides (see page 7, 1st column line 30-36). Southern teaches that the use of glass has the advantages that liquid cannot penetrate glass, it enhances the rate of hybridization, improves washing by improving diffusion.

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the treated glass support taught by Southern as the solid support of Haung in view of Voelker. The ordinary artisan would be motivated to use the treated glass support of Southern because Southern teaches glass improves washing; rate of hybridization and liquid cannot penetrate it. The use of the treated glass taught by Southern would thus allow more efficient assays.

Summary

No claims are allowed over prior art cited.

Conclusions

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven C. Pohnert whose telephone number is 571-272-3803. The examiner can normally be reached on Monday-Friday 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Steven Pohnert

JEANNINE A. GOLDBERG
PRIMARY EXAMINER
1/19/07